REMARKS

Claims 1-24 and 26-40 are pending in the application; claim 25 has been canceled; claims 35-40 are withdrawn from consideration following a restriction requirement and election of claims; claims 1-24 and 26-34 are under prosecution.

The Examiner has withdrawn the earlier rejections and presented new grounds for rejection, explaining that the new grounds for rejection were necessitated by the Applicant's amendments. The Applicant requests reconsideration of the final rejection in view of the amendments and remarks in this paper; it is also hoped that the amendments will be entered.

Claim 6 stands rejected under 35 U.S.C. 112, second paragraph. The claims has been amended, as recommended by the Examiner, to overcome the rejection. The rejection should now be withdrawn.

Claims 1-11, 15-24, 27-29 and 31-34 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) in view of McGall et al (U.S. Patent No. 6,147,205, filed 5 March 1997).

Regarding Claim 1, the Examiner contends that Walt et al. disclose a coating composition comprising a gelling agent and microspheres dispersed in a fluid (i.e. solution, page 22, lines 9-22) wherein upon coating the composition on a substrate, said microspheres become immobilized in the plane of coating and form a random pattern on the substrate i.e. the microspheres are within a solution which upon evaporation (gelling) holds the microspheres in place (page 22, lines 15-16) wherein the gelling agent is selected from polyethylene glycol and polyacrylamide (page 22, lines 20-22) which are defined by the specification as gelling agents.

The Applicant respectfully traverses the rejection. Before addressing the rejection specifically, the Applicant will briefly discuss the advantages and distinction of his invention over the art.

Prior to the present invention, practitioners in the microarray technology would prepare substrates for receiving microspheres at preselected sites. This they did by creating areas on the surface of the substrate (e.g., microwells or chemical moieties) where the microspheres would be specifically positioned or chemically attracted. The present invention has improved the

technology by providing a unique coating composition that can be coated on a substrate that has not been etched with microwells or chemically modified or otherwise prepared to receive the microspheres at specific sites; nevertheless the microspheres remain immobilized on the substrate. The present invention provides a microarray that is less costly and easier to prepare than those heretofore disclosed because it makes such substrate preparation unnecessary, yet allowing a desirable distribution of microspheres on the substrate. *See,* page 3 of the application.

The inventor has used the term "random distribution" to distinguish over the predetermined pattern that is directed by the prior art methods. On page 5, line 16-26, it is explained :

> *As used herein, the term "random distribution" means a spatial distribution of elements showing no preference or bias. Randomness can be measured in terms of compliance with that which is expected by a Poisson distribution.*
> *The present invention teaches a composition and a method for making a random array of microspheres, also referred to as "beads", on a substrate. The distribution or pattern of the microspheres on the substrate is entirely random and the microspheres are not attracted or held to sites that are pre-marked or predetermined on the substrate as in other methods previously disclosed. In the present invention, the microspheres are immobilized randomly when the gelling agent in which they are carried undergoes a sol-to-gel transition.*

Turning now to the Examiner's rejection, on p.3 of the Office Action the examiner states: "Regarding claim 1, Walt et al. disclose a coating composition comprising a gelling agent and micro-spheres dispersed in a fluid (p.22 lines 9-22) wherein upon coating the composition on a substrate, said micro-spheres become immobilized in the plane of the coating and form a random pattern on the substrate i.e. the micro-spheres are within a solution which upon evaporation (gelling) holds the micro-spheres in place..."

The Applicant disagress with the Examiner's interpretation of what Walt et al. is teaching. A detailed reading of that reference reveals the following: "The placement of micro-spheres may be accomplished by dripping a solution containing the desired randomly mixed subpopulations of the micro-spheres over

the distal end 212, sonicating the bundle to settle the micro-spheres in the wells, and allowing the micro-sphere solvent to evaporate." (Page 22, lines 9-22, emphasis added).

The passage quoted above does not teach a gelling agent in the solution containing the micro-spheres, as is taught in the present application. The Applicant maintains, and can present evidence if necessary, that a random +distribution of micro-spheres cannot be preserved upon evaporation of the fluid of Walt et al. in the absence of patterning (or wells) without the presence of a gelling agent. In contrast, the absence of such wells is an important feature of the present invention.

Walt et al. continues: "Micro-spheres 10 may then be fixed into the wells 250 by using a dilute solution of sulfonated Nafion that is dripped over the end. Upon evaporation, a thin film of Nafion was formed over the micro-spheres which holds them in place." It is clear from this reading that the film-forming polymer is added separately and later on to fix the micro-spheres in the wells. The polymer is used here as a film-forming polymer and not as a component of a fluid that undergoes thermally induced sol-gel transition. The coating composition of the present invention is fundamentally different.

Furthermore, by using the expression "evaporation (gelling)", it appears that the Examiner interprets the terms to be synonyms . This is not so; certainly not in this instance. Evaporation and gelling refer to completely different phenomena. Evaporation is the conversion of a liquid to a vapor whereas gelling or gelation is the formation of a gel from a sol. Gelation is an important phenomenon in the present invention and for this reason is defined in the specification at p.4, line 20, of the present application.

The Examiner combines Walt et al. with Mc Gall et al., arguing that while Walt et al. do not teach coating aids, Mc Gall et al do and that it would have been obvious to combine the teachings.

The Applicant traverses the rejection because, firstly, even with a coating aid added to the composition of Walt et al., one still does not arrive at the composition of the invention, for the reasons already discussed above. In the arguments above, the Applicant relied on other differences between the reference and the invention – differences that are even more substantial than the presence of a coating aid.

Secondly, Mc Gall et al. do not teach polyethylene glycol. That reference lists other agents, for example polyvinyl alcohol, which has been shown to be unsuitable for the purposes of the present invention. *See*, Control Formulation 2 on page 9 of the application. In fact, the application teaches at page 5, lines 2-5 that polyvinyl is not useful for the present invention unless it is cross-linked. The Applicant maintains that sol-gel transition is need for the invention. The combination of Mc Gall et al. and Walt et al. therefore does not make the invention obvious.

Regarding Claim 2, the Examiner argues that the instantly claimed "useful for coating" is a recitation of intended use for the composition and this does not differentiate the claimed product from a Prior art product if the prier art product teaches all the structural limitations of the claim. Ex parte Masham, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987). However, for the reasons discussed above, Walt et al. and McGall et al. do not teach all the structural limitations of the claimed composition and therefore, do not teach the claimed composition.

Regarding Claim 3, the Examiner contends that Walt et al. disclose the composition wherein the random pattern is preserved (i.e. held in place) upon gelling of the gelling agent (page 22, lines 15-16).

The Applicant reiterates here what was discussed above, namely, that "random" as described in the text of the instant application is very different from what Walt et al. disclosed. Microspheres positioned in microwells designed on a substrate are not in a "random" position for purposes of the application. To distinguish this feature in the invention, the Applicant has amended claim 1 to recite "random: in the preamble.

Regarding Claim 28, the examiner states that Walt et al. disclose the micro-array wherein the substrate is free of receptors designed to physically interact with the micro-spheres i.e. the substrate is planar and therefore free of receptors (wells) for physical interaction with the micro-spheres. But Walt et al state the following (p.7 lines 14-32) " Generally the substrate is planar, although as will be appreciated by those in the art, other configurations of substrates may be used as well; for example, three-dimensional configurations can be used, for example by embedding the beads in a porous block of plastic.." At least the surface of the substrate is modified to contain discrete individual sites for later association of micro-spheres. Clearly, the fact that the substrate is planar does not

mean that the substrate is free of receptors. The word planar here is used to distinguish a two-dimensional substrate from a three-dimensional substrate.

The Examiner later on states that Walt et al. teach that the "substrate .... can be modified to contain discrete individual sites" and goes on to state that Walt et al. teach that "Generally the substrate is planar". It should be pointed out that on line 21 of the same page Walt et al. teach that at least one surface of the substrate is modified to contain discrete, individual sites for later association of micro-spheres. Furthermore, as stated previously use of the word "planar" by Walt et al. does not imply absence of receptors.

The Examiner also states " Regarding Claim 34, Walt et al disclose the micro-array wherein the substrate is flexible i.e. optical fiber. Applicant would like to point out that an optical fiber does not constitute a flexible substrate for web coating.

The claims dependent on claim 1 bear all the features described in claim 1 and the Applicant maintains that claim 1 is novel and unobvious over Walt et al. and Mc Gall et al., alone or combined. The dependent claims are therefore patentable.

Claims 1-8, 12-13, 24 and 27-34 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (U.S. Patent Application Publication No. 2002/0015952, filed 1 February 2001) in view of McGall et al. (U.S. Patent No. 6,147,205, filed 5 March 1997).

The Applicant traverses the rejection and reiterates what was said earlier concerning Anderson et al. Anderson et al. (U.S. Patent Application No. 2002/0015952) discloses a method of preparing a micro-array wherein micro-spheres with attached biological probes are dispersed in a gelling agent such as gelatin. The composition in a fluid (sol) state is sucked into a bundle of tubules (approx. 1mm internal diameter) and allowed to chill set (sol-gel transition). The bundle of tubules is then cross-sectioned using a micro-tome and attached to a plane surface (having no preselected sites) to form an array of discs having a thickness of about 5 to 20 microns. The material making up the walls of the tubules may be selectively removed leaving behind a group of 'islands' or 'pillars' on the surface.

The application does not teach spreading the micro-spheres uniformly on the surface in the fluid state prior to immobilization via a sol to gel

transition of the medium. It teaches creating structures having *three-dimensional form* (# **142**) or *small pillars with a gap between them* (#**143**). Hence, the microspheres are not immobilized randomly on the substrate on gelation of the gelling agent. In one embodiment cited by the Examiner (#**134**) it is possible to directly transfer material to a surface to create these 'pillars'. However, the material is transferred "*as a paste or a gel that remains firm or quickly hardens after being extruded onto a solid phase*". Again, in (#**145**) it is stated that:

> *other techniques for producing a three-dimensional structure include depositing a three-dimensional structure directly on the solid surface. This may involve a preformed structure of a fluid or semi-fluid material which solidifies very quickly before it spreads significantly....*

Anderson et al. clearly teaches away from creating a uniform spreading layer of micro-spheres on the surface by using coating aids or spreading agents as disclosed in Example 1 of the present application. Uniformity of coating of the micro-spheres is emphasized again in Example 2 of the application. The cited references, McGall et al. and Anderson et al., do not use coating aids because they are not spreading a coating as is the Applicant. In fact, Anderson et al. do not want spreading. As cited immediately above, Anderson et al. aim at having the gel solidify on the substrate *before it spreads significantly*. By adding McGall et al. (for its coating aid) to Anderson et al., the Examiner, for the purpose of arguing obviousness, has destroyed the express aim and feature of the invention of Anderson et al.; in fact such a combination would cause the Anderson et al. invention to fail.

Furthermore, Figure 3 in Anderson et al. shows that the beads form a three-dimensional structure on the substrate, which is to be expected since, as stated in paragraph #145, a three-dimensional structure can be deposited directly on the substrate and allowed to solidify very quickly before it spreads significantly. Applicant requests that the rejection be withdrawn.

Claims 12-14 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) in view of McGall et al (U.S. Patent No. 6,147,205, filed 5 March 1997) as applied to Claims 1 and 27 above and further in view of Anderson et al (U.S. Patent Application Publication No. 2002/0015952, filed 1 February 2001).

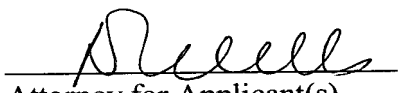
The Applicant traverses the rejection. Walt et al. do not teach a gelling agent as described in the application and even the combined references do not teach a random immobilization on the substrate upon gelation of the gelling agent. The rejection should be withdrawn.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al. in view of McCall et al. 6,1.47,?OS, filed 5 March 1997) as applied to Claims 1 and 27 above and further in view of Chang et al. (U.S. Patent No. 4,873,102, issued 10 October 1989).

The Applicant traverses the rejection and reiterates the novelty of. Claim 26 is therefore also novel.

In view of the foregoing amendments and remarks, reconsideration of this patent application is respectfully requested. A prompt and favorable action by the Examiner is earnestly solicited. Should the Examiner believe any remaining issues may be resolved via a telephone interview, the Examiner is encouraged to contact Applicants' representative at the number below to discuss such issues.

Respectfully submitted,



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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A coating composition for making a random microarray comprising:

microspheres dispersed in a fluid, the fluid containing a coating aid and a gelling agent or a precursor to a gelling agent, wherein the microspheres are immobilized at random positions on a substrate upon gelation of the gelling agent.

2. (previously presented) A coating composition according to claim 1 useful for coating on a substrate that is not premarked and does not contain microwells.

3 (original) A coating composition according to claim 1 wherein the random pattern on the substrate is preserved upon gelation of the gelling agent.

4. (previously presented) A coating composition according to claim 1 wherein the microspheres are chemically functionalized to have surface active sites.

5. (previously presented) A coating composition according to claim 4 wherein the surface active sites carry organic or inorganic attachments.

6. (currently amended) A coating composition according to claim 4 wherein organic or inorganic attachments on ~~the~~ a surface active site are capable of chemical or physical interaction.

7. (original) A coating composition according to claim 4 wherein the surface active site is bioactive.

8. (original) A coating composition according to claim 7 wherein the bioactive site interacts with nucleic acid, protein, or fragments thereof.

9. (original) A coating composition according to claim 1 wherein the microsphere contains a signature.

10. (original) A coating composition according to claim 9 wherein the signature is comprised of an oil-soluble dye.

11. (original) A coating composition according to claim 9 wherein the signature is interrogatable by optical, magnetic, or other electromagnetic means.

12. (original) A coating composition according to claim 1 wherein the gelling agent is gelatin.

13. (original) A coating composition according to claim 1 wherein the gelling agent undergoes thermal gelation.

14. (original) A coating composition according to claim 12 wherein the gelatin is alkali pretreated gelatin.

15. (original) A coating composition according to claim 1 wherein the microspheres have a mean diameter between 1 and 50 microns.

16. (original) A coating composition according to claim 1 wherein the microspheres have a mean diameter between 3 and 30 microns.

17. (original) A coating composition according to claim 1 wherein the microspheres have a mean diameter between 5 and 20 microns.

18. (original) A coating composition according to claim 1 wherein the microspheres in the composition are immobilized on the substrate in a concentration between 100 and 1 million microspheres per cm2.

19. (original) A coating composition according to claim 1 wherein the microspheres in the composition are immobilized on the substrate in a concentration between 1000 and 200,000 microspheres per cm2.

20. (original) A coating composition according to claim 1 wherein the microspheres in the composition are immobilized on the substrate in a concentration between 10,000 and 100,000 microspheres per cm2.

21. (original) A coating composition according to claim 1 wherein the microspheres comprise a synthetic or natural polymeric material.

22. (original) A coating composition according to claim 21 wherein the polymeric material is an amorphous polymer.

23. (original) A coating composition according to claim 22 wherein the amorphous polymer is polystyrene.

24. (original) A coating composition according to claim 4 wherein the microsphere contains a surface active site comprising a functionality selected from the group consisting of carboxy, amine, epoxy, hydrazine, aldehyde and combinations thereof.

25. (canceled)

26 (original) A coating composition according to claim 1 wherein the microspheres are prepared by emulsion polymerization or limited coalescence.

27. (previously presented) A microarray comprising:

a substrate coated with a composition comprising microspheres dispersed in a fluid, the fluid containing a coating aid and a gelling agent or a precursor to a gelling agent, wherein the microspheres are immobilized at random positions on the substrate upon gelation of the gelling agent.

28. (original) A microarray according to claim 27 wherein the substrate is free of receptors designed to physically or chemically interact with the microspheres.

29. (original) A microarray according to claim 27 wherein the random pattern on the substrate is preserved upon gelation of the gelling agent.

30. (original) A microarray according to claim 27 wherein the gelling agent is gelatin.

31. (original) A microarray according to claim 27 wherein the microspheres bear chemically active sites.

32. (original) A microarray according to claim 27 wherein the chemically active site is bioactive.

33. (original) A microarray according to claim 27 wherein the substrate comprises glass, plastic, cellulose acetate, or polyethyleneterephthalate.

34. (currently amended) A microarray according to claim ~~25~~ 27 wherein the substrate is flexible.

35.-40. (withdrawn)

41. (new) A coating composition for making a random microarray comprising:

microspheres dispersed in a fluid, the fluid containing a coating aid and a gelling agent or a precursor to a gelling agent, said fluid being capable of sol-to-gel transition; and wherein the microspheres are immobilized at random positions on a substrate when said sol-to-gel transition occurs.

42. (new) A microarray comprising:

a substrate coated with a composition comprising microspheres dispersed in a fluid, the fluid containing a coating aid and a gelling agent or a precursor to a gelling agent, said fluid being capable of sol-to-gel transition; and

wherein the microspheres are immobilized at random positions on the substrate when said sol-to-gel transition occurs.